Visual Acuity, Vitreous Hemorrhage, and Other Ocular Outcomes After Vitrectomy vs Aflibercept for Vitreous Hemorrhage Due to Diabetic Retinopathy

A Secondary Analysis of a Randomized Clinical Trial

Adam R. Glassman, MS,[1] Wesley T. Beaulieu, PhD,[1] Maureen G. Maguire, PhD,[2] Andrew N. Antoszyk, MD,[3] Clement C. Chow, MD,[4] Michael J. Elman, MD,[5] Lee M. Jampol, MD,[6] Hani Salehi-Had, MD,[7] and Jennifer K. Sun, MD, MPH[8], for the DRCR Retina Network
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Key Points

Questions

Among eyes with vitreous hemorrhage due to proliferative diabetic retinopathy initially treated with aflibercept or vitrectomy with panretinal photocoagulation, what changes occur in visual acuity and other ocular outcomes?

Findings

In this comparative effectiveness study of 205 eyes undergoing treatment, no difference in mean visual acuity over 24 weeks was noted

between treatment groups. Results of post hoc analyses show that the vitrectomy group had better visual acuity over 24 weeks of follow-up in the subgroup of eyes with baseline best-corrected visual acuity worse than 20/800.

Meaning

Aflibercept and vitrectomy are viable treatment options for vitreous hemorrhage due to proliferative diabetic retinopathy, and the results of this study may influence treatment decisions when initiating therapy.

This secondary analysis of a randomized clinical trial compares exploratory outcomes between treatment groups that may affect treatment choices for patients with vitreous hemorrhage due to proliferative diabetic retinopathy.

Abstract

Importance

Although there were no differences in mean visual acuity (VA) over 24 weeks after vitrectomy with panretinal photocoagulation (PRP) vs aflibercept in a randomized clinical trial among eyes with vitreous hemorrhage due to proliferative diabetic retinopathy (PDR), post hoc analyses may influence treatment choices.

Objective

To compare exploratory outcomes between treatment groups that may affect treatment choices for patients with vitreous hemorrhage due to PDR.

Design, Setting, and Participants

This post hoc analysis of a randomized clinical trial conducted at 39 DRCR Retina Network sites included adults with vision loss due to PDR-

related vitreous hemorrhage for whom vitrectomy was considered. Data were collected from November 2016 to January 2020.

Interventions

Random assignment to 4 monthly injections of aflibercept vs vitrectomy with PRP. Both groups could receive aflibercept or vitrectomy during follow-up based on protocol-specific criteria.

Main Outcomes and Measures

Visual acuity area under the curve (adjusted for baseline VA) and clearance of vitreous hemorrhage.

Results

A total of 205 eyes were included in the analysis (115 male [56%] and 90 [44%] female participants; mean [SD] age, 57 [11] years). Among 89 eyes with a baseline VA of 20/32 to 20/160 (47 receiving aflibercept, including 4 [9%] that had undergone vitrectomy; 42 undergoing vitrectomy, including 3 [7%] that had received aflibercept), the adjusted mean difference in VA letter score over 24 weeks between the aflibercept and vitrectomy groups was −4.3 (95% CI, −10.6 to 1.9) compared with −16.7 (95% CI, −24.4 to −9.1) among 59 eyes with baseline VA worse than 20/800 ($P = .02$ for interaction; 26 in the aflibercept group, including 6 [23%] that had undergone vitrectomy; 33 in the vitrectomy group, including 8 [24%] that had received aflibercept). In the full cohort, the median time to clearance of the initial vitreous hemorrhage was 36 (interquartile range [IQR], 24-52) weeks in the aflibercept group vs 4 (IQR, 4-4) weeks in the vitrectomy group (difference, 32 [95% CI, 20-32] weeks; $P < .001$).

Conclusions and Relevance

Both initial aflibercept and vitrectomy with PRP are viable treatment approaches for PDR-related vitreous hemorrhage. Although this study did

not find a significant difference between groups in the primary outcome of mean VA over 24 weeks of follow-up, eyes receiving initial vitrectomy with PRP had faster recovery of vision over 24 weeks when baseline VA was worse than 20/800 and faster vitreous hemorrhage clearance. Approximately one-third of the eyes in each group received the alternative treatment (aflibercept or vitrectomy with PRP). These factors may influence treatment decisions for patients initiating therapy for PDR-related vitreous hemorrhage.

Trial Registration

ClinicalTrials.gov Identifier: NCT02858076

Introduction

Vitreous hemorrhage is common in patients with proliferative diabetic retinopathy (PDR) and can cause severe vision loss.[1] Despite treatment with panretinal photocoagulation (PRP) or intravitreous ranibizumab for PDR, almost half of the eyes in the DRCR Retina Network Protocol S developed vitreous hemorrhage during 5 years of follow-up.[2] Although vitreous hemorrhage can clear spontaneously, intervention may hasten visual recovery. Once the clinician and patient decide that intervention for the vitreous hemorrhage is needed, treatment options include injections of anti–vascular endothelial growth factor (anti-VEGF) agents to cause regression of neovascularization while the vitreous hemorrhage is reabsorbed or surgical removal of the vitreous hemorrhage and neovascular membranes with vitrectomy plus PRP.

The DRCR Retina Network Protocol AB compared eyes with vitreous hemorrhage due to PDR randomly assigned to initial intravitreous aflibercept injections or vitrectomy with PRP wherein eyes in both groups could receive aflibercept or vitrectomy during follow-up based on protocol-specific criteria.[3] In Protocol AB, the mean visual acuity (VA) letter score over 24 weeks of follow-up (area under the curve) was 59.3 (Snellen equivalent, 20/63) in the aflibercept group vs 63.0 (Snellen

equivalent, 20/63) in the vitrectomy group (adjusted difference, –5.0 [95% CI, –10.2 to 0.3]; *P* = .06). At 4 weeks, the mean VA was significantly better in the vitrectomy group; however, starting at the 12-week visit and over 2 years, VA was not significantly different between the groups. Per protocol, approximately one-third of the eyes assigned to aflibercept received vitrectomy and approximately one-third of eyes assigned to vitrectomy received aflibercept after vitrectomy over 2 years.

The primary results of Protocol AB demonstrated similar long-term VA outcomes and reasonable safety profiles when initiating treatment with either aflibercept or vitrectomy with PRP (eTable 1 in the Supplement).[3] This report provides additional details on the DRCR Retina Network treatment regimens for the Protocol AB groups receiving aflibercept and vitrectomy with PRP and post hoc ocular outcomes that might influence treatment decisions for individual patients.

Methods

The study procedures have been reported previously.[3] The study adhered to the tenets of the Declaration of Helsinki.[4] Study participants provided written informed consent. The protocol was approved by the ethics board associated with each study site and is available on the DRCR Retina Network website.[5] Participants were recruited at 39 clinical sites in the US. Study eyes had VA impairment (Snellen equivalent, 20/32 or worse) owing to PDR-related vitreous hemorrhage for which treatment was indicated. Eyes with traction retinal detachment were allowed if the detachment did not involve or threaten the macula. Eyes were randomly assigned to initial intravitreous injections of aflibercept, 2 mg (EYLEA, Regeneron), or vitrectomy with PRP. Data were collected from November 2016 to January 2020.

Aflibercept Treatment Regimen

Eyes assigned to aflibercept received 4 monthly injections starting at baseline. Eyes received 2 additional injections unless neovascularization

was absent with a clear view of the fundus at the 16- or 20-week visit, in which case injections were deferred (eFigure 1 in the Supplement). Thereafter, injections continued if the eye was improving or worsening with respect to vitreous hemorrhage and neovascularization. Injections were deferred when the vitreous hemorrhage and neovascularization stabilized (defined as no change since the last visit in the size and density of the hemorrhage and neovascularization on clinical examination after ≥2 consecutive injections). Vitrectomy was not performed within the first 16 weeks after initial aflibercept treatment unless 1 of the following serious adverse events occurred: retinal detachment involving or threating the macula, angle neovascularization, progressive iris neovascularization, or uncontrolled intraocular pressure from neovascular glaucoma or ghost cell glaucoma. Vitrectomy could be performed at the investigator's discretion if vision-impairing vitreous hemorrhage was present after 16 weeks and 2 consecutive monthly injections. If vitrectomy was performed, the procedure was the same as that for eyes randomly assigned to vitrectomy, including application of intraoperative PRP.

Vitrectomy Treatment Regimen

Vitrectomy was performed per the investigator's usual routine. The only protocol requirements were a 23-gauge or smaller vitrectomy system, no intraoperative aflibercept, and complete PRP during surgery (defined as 500-µm burns on the retina placed ≤1 to 2 burn widths apart beginning approximately 3000 µm from the macular center and extending at least to the equator in all directions). Aflibercept was permitted within 1 to 14 days before surgery but was prohibited during surgery and through 4 weeks after surgery. Cataract extraction and epiretinal or internal limiting membrane peeling were performed at the surgeon's discretion.

If vitreous hemorrhage recurred 4 weeks after vitrectomy or later, aflibercept was given to clear the hemorrhage without additional surgery. If the hemorrhage persisted after 2 monthly aflibercept injections, repeat vitrectomy or additional aflibercept injections were performed at the investigator's discretion. Aflibercept also could be given if

neovascularization persisted.

Outcomes

The main between-group outcome was the difference in mean VA letter score between treatment groups by baseline VA over 24 weeks (area under the curve; primary outcome in Protocol AB) and at 4, 12, 24, 52, and 104 weeks. Subgroups were chosen post hoc to have similar sample size and were defined as having a VA of 20/32 to 20/160 (letter score, 78-39), 20/200 to 20/800 (letter score, 38-4), and worse than 20/800 (letter score, ≤3). Additional between-group outcomes included the occurrence of any of the following over 2 years: VA of 20/25 or better (letter score, ≥79), clearance of initial vitreous hemorrhage, resolution of retinal neovascularization, or cataract extraction. Presence of vitreous hemorrhage and neovascularization (defined as neovascularization of the disc or elsewhere) were assessed by investigators on clinical examination. Within-group outcomes included presence of traction retinal detachment during initial vitrectomy by timing of preoperative aflibercept injection (vitrectomy group only), presence of vitreous hemorrhage by visit, VA after recurrent vitreous hemorrhage, VA by presence of retinal neovascularization at 4 and 104 weeks, and VA before and after cataract extraction.

Statistical Methods

Outcomes were evaluated post hoc and should be considered exploratory. Two-sided $P < .05$ indicated significance. There was no adjustment for multiplicity. Analyses of mean VA were conducted via robust regression using M-estimation and the bisquare weight function with covariate adjustment for baseline VA and lens status. Time-to-event outcomes were compared between treatment groups with the log-rank test, cumulative probabilities were calculated using the product-limit estimator, and 95% CIs for the difference in median time to event were calculated via bootstrapping. Analyses were conducted with SAS software, version 9.4 (SAS Institute Inc).

Results

VA Outcomes

Among the 205 eyes included (115 male [56%] and 90 female [44%] participants; mean [SD] age, 57 [11] years), the median baseline VA letter score was 37.0 (interquartile range [IQR], 63.0-0.0; Snellen equivalent, 20/200) in the study eye and 78.0 (IQR, 84.0-68.0; Snellen equivalent, 20/32) in the fellow eye. Among fellow eyes, VA was worse than the study eye in 13 (6%) and worse than 20/40 in 54 (26%).

The mean VA over 24 weeks was better for the vitrectomy vs aflibercept groups when baseline VA was worse than 20/800 but not when baseline VA was better (*P* = .02 for interaction) (Figure 1 and eTable 2 in the Supplement). Among eyes with a baseline VA of 20/32 to 20/160, the mean VA letter score over 24 weeks in the aflibercept group (n = 47) was 72.2 (95% CI, 76.5-68.0; Snellen equivalent, 20/40) vs 76.6 (95% CI, 81.1-72.1; Snellen equivalent, 20/32) in the vitrectomy group (n = 42) (adjusted difference, −4.3 [95% CI, −10.6 to 1.9]). Among eyes with a baseline VA of 20/200 to 20/800, the mean VA letter score over 24 weeks in the aflibercept group (n = 24) was 60.1 (95% CI, 66.1-54.2; Snellen equivalent, 20/63) vs 63.6 (95% CI, 69.7-57.6; Snellen equivalent, 20/63) in the vitrectomy group (n = 23) (adjusted difference, −3.5 [95% CI, −12.0 to 5.0]). Among eyes with a baseline VA worse than 20/800, the mean VA letter score over 24 weeks in the aflibercept group (n = 26) was 48.4 (95% CI, 54.1-42.7; Snellen equivalent, 20/125) vs 65.1 (95% CI, 70.2-60.0; Snellen equivalent, 20/50) in the vitrectomy group (n = 33) (adjusted difference, −16.7 [95% CI, −24.4 to −9.1]).

Figure 1.

Mean Visual Acuity (VA) Over 2 Years by Treatment Group and Baseline VA Subgroup

Error bars represent 95% CIs. Best-corrected VA was collected after protocol-defined refraction. Visual acuity was measured with the electronic Early Treatment Diabetic Retinopathy Study VA test on a scale from 100 (Snellen equivalent, 20/10) to 0 letters (Snellen equivalent, worse than 20/800). PRP indicates panretinal photocoagulation.

The effect of baseline vision on VA over 24 weeks was driven by

differences at 4 weeks (eTable 2 in the Supplement). The adjusted mean difference in VA letter score between treatment groups at 4 weeks was −6.9 (95% CI, −15.6 to 1.8) among eyes with a baseline VA of 20/32 to 20/160, −8.4 (95% CI, −20.8 to 4.1) among eyes with a baseline VA of 20/200 to 20/800, and −42.9 (95% CI, −54.2 to −31.6) among eyes with a baseline VA worse than 20/800. For interaction between baseline VA and treatment group on VA at 4 weeks, the difference was significant at $P <$ .001, compared with $P = .84$ at 12 weeks, $P = .28$ at 24 weeks, $P = .74$ at 52 weeks, and $P = .66$ at 104 weeks. The distribution of VA by baseline VA and visit is shown in eFigure 2 in the Supplement.

The probability of achieving VA of 20/25 or better over 4 weeks was 16% (95% CI, 10%-25%) in the aflibercept group and 30% (95% CI, 23%-40%) in the vitrectomy group (difference, −14% [95% CI, −26% to −3%]); over 2 years, the probability was 78% (95% CI, 70%-86%) in the aflibercept group and 70% (95% CI, 61%-79%) in the vitrectomy group (difference, 8% [95% CI, −4% to 20%]; $P = .60$) (eFigure 3 in the Supplement). The interaction between baseline VA and treatment was not significant with $P = .38$ (eFigure 4 in the Supplement).

Treatment During Follow-up

Over 2 years in the aflibercept group, vitrectomy was performed in 11 of 48 eyes (23%) with a baseline VA of 20/32 to 20/160, 6 of 26 eyes (23%) with a baseline VA of 20/200 to 20/800, and 16 of 26 eyes (62%) with a baseline VA of worse than 20/800. Before 24 weeks, the rates were 4 of 47 (9%) for VA of 20/32 to 20/160, 4 of 24 (17%) for VA of 20/200 to 20/800, and 6 of 26 (23%) for VA of worse than 20/800. In the vitrectomy group, aflibercept was given after vitrectomy over 2 years in 14 of 48 eyes (29%) with a baseline VA of 20/32 to 20/160, 7 of 24 eyes (29%) with a baseline VA of 20/200 to 20/800, and 13 of 33 eyes (39%) with a baseline VA worse than 20/800; before 24 weeks, the rates were 3 of 42 (7%) for VA of 20/32 to 20/160, 2 of 23 (9%) for VA of 20/200 to 20/800, and 8 of 33 (24%) for VA worse than 20/800.

Traction Retinal Detachment and Use of Aflibercept Before Vitrectomy

Forty-four of 105 eyes (42%) in the vitrectomy group received aflibercept a median of 6 days before the initial vitrectomy. Traction retinal detachments were noted during surgery in 5 of 26 eyes (19%) that received aflibercept 6 or fewer days before initial vitrectomy, 3 of 18 eyes (17%) that received aflibercept 7 or more days before vitrectomy, and 7 of 59 eyes (12%) that did not receive aflibercept before vitrectomy.

Vitreous Hemorrhage

Based on clinician assessment, vitreous hemorrhage was present at 24 weeks in 61 of 95 eyes in the aflibercept group (64%) and 10 of 97 eyes in the vitrectomy group (10%) ($P<.001$) (Figure 2). At 2 years, vitreous hemorrhage was present in 34 of 89 eyes in the aflibercept group (38%) and 3 of 86 eyes in the vitrectomy group (3%) ($P<.001$). The median time to clearance of initial vitreous hemorrhage was 36 (IQR, 24-52) weeks in the aflibercept group vs 4 (IQR, 4-4) weeks in the vitrectomy with PRP group (difference, 32 [95% CI, 20-32] weeks; $P<.001$) (Figure 3).

Figure 2.

Presence of Vitreous Hemorrhage Over 2 Years by Treatment Group

Presence of vitreous hemorrhage was assessed by the investigator during clinical examination. Error bars represent 95% CIs for the proportion of eyes with vitreous hemorrhage. PRP indicates panretinal photocoagulation.

Figure 3.

Time to Clearance of Initial Vitreous Hemorrhage by Treatment Group

Presence of vitreous hemorrhage was assessed by the investigator during clinical examination. PRP indicates panretinal photocoagulation.

The cumulative probability of recurrent hemorrhage (after initial vitreous hemorrhage clearance) over 2 years was 53% (95% CI, 43%-63%) in the aflibercept group vs 17% (95% CI, 11%-26%) in the vitrectomy group (difference, 36% [95% CI, 23%-48%]; $P<.001$) (eFigure 5 in the Supplement). The median change in VA letter score from the visit before the first recurrent hemorrhage to the visit with recurrent hemorrhage was

−6.0 (IQR, −26.0 to 0.0) in the aflibercept group (n = 51) and −31.0 (IQR, −78.0 to −6.0) in the vitrectomy group (n = 17). At 104 weeks, the median VA letter score among eyes that had recurrent hemorrhage during follow-up was 78.0 (IQR, 85.0-67.0; Snellen equivalent, 20/23) in the aflibercept group (n = 46) and 71.5 (IQR, 80.0-5.0; Snellen equivalent, 20/40) in the vitrectomy group (n = 14); among eyes without recurrent vitreous hemorrhage, the median VA letter score was 76.5 (IQR, 85.0-62.0; Snellen equivalent, 20/32) in the aflibercept group (n = 44) and 80.0 (IQR, 85.0-72.0; Snellen equivalent, 20/25) in the vitrectomy group (n = 73).

Retinal Neovascularization

The median time to resolution of retinal neovascularization over 2 years was 12 (IQR, 12-24) weeks with aflibercept vs 4 (IQR, 4-12) weeks with vitrectomy (difference, 8 [95% CI, 8-8] weeks; $P < .001$) (Figure 4). Eyes could not be fully assessed for retinal neovascularization at 151 of 1509 visits (10%; due to vitreous hemorrhage in 127 cases [84%]). The percentage of eyes with retinal neovascularization by visit and group is shown in Figure 5. In the aflibercept group, the median VA letter score at 4 weeks among eyes with retinal neovascularization (n = 31) was 72.0 (IQR, 80.0-54.0; Snellen equivalent, 20/40) vs 71.5 (IQR, 77.0-66.0; Snellen equivalent, 20/40) among eyes without retinal neovascularization (n = 22). Among 42 eyes in which neovascularization could not be assessed, the median VA letter score was 47.5 (IQR, 62.0-0.0; Snellen equivalent, 20/125). At 104 weeks in the aflibercept group, the median VA letter score among eyes with retinal neovascularization (n = 20) was 78.5 (IQR, 84.0-68.0; Snellen equivalent, 20/32) vs 78.0 (IQR, 85.5-65.0; Snellen equivalent, 20/32) among eyes without neovascularization (n = 68).

Figure 4.

Time to Resolution of Retinal Neovascularization by Treatment Group

Retinal neovascularization was defined as neovascularization of the disc or elsewhere as assessed by the investigator during clinical examination. PRP indicates panretinal photocoagulation.

Figure 5.

Presence of Retinal Neovascularization Over 2 Years by Treatment Group

Presence of retinal neovascularization was assessed by the investigator during clinical examination. Error bars represent 95% CIs for the proportion of eyes with retinal neovascularization. Retinal neovascularization could not be assessed at 4, 12, 24, 36, 52, 68, 84, and 104 weeks in 42, 25, 12, 5, 6, 9, 7, and 2 eyes in the aflibercept group and 15, 7, 6, 2, 3, 4, 2, and 4 eyes in the vitrectomy with PRP group, respectively (these eyes are excluded from the denominator of the percentage).

Cataract Extraction

Among eyes that were phakic at baseline (75 in the aflibercept group and 81 in the vitrectomy group), the cumulative probability of cataract extraction by 2 years was 31% (95% CI, 22%-43%) in the aflibercept group vs 28% (95% CI, 19%-40%) in the vitrectomy with PRP group (difference, 2% [95% CI, –13% to 17%]; *P* = .81) (eFigure 6 in the Supplement). The median VA letter score gain from the visit preceding cataract extraction to the visit after cataract extraction was 19.0 (IQR, 5.0-31.0) in the aflibercept group (n = 22) and 11.0 (IQR, 1.0-31.0) in the vitrectomy group (n = 21) (eTable 3 in the Supplement). At 104 weeks, the median VA letter score among eyes that underwent cataract extraction during the study was 78.0 (IQR, 83.0-65.0; Snellen equivalent, 20/32) in the aflibercept group (n = 21) and 78.5 (IQR, 86.0-55.0; Snellen equivalent, 20/32) in the vitrectomy group (n = 20).

Discussion

Although the vitrectomy group experienced faster visual recovery than the aflibercept group, especially among the post hoc subgroup of eyes with a baseline VA of worse than 20/800 (59 of 205 eyes, or 29% of the cohort), visual recovery after 24 weeks and over 2 years was not significantly different between groups regardless of baseline VA. The potential advantages of initial vitrectomy include faster clearance of initial vitreous hemorrhage, lower rate of recurrent vitreous hemorrhage, and avoidance of aflibercept injections in approximately two-thirds of eyes. The potential advantages of initial aflibercept include avoidance of vitrectomy in approximately two-thirds of eyes and similar VA from 12 weeks onward. Rates of cataract extraction were not significantly different between the groups.

The process of choosing a treatment approach for an individual is multifaceted. However, the effect on VA, both in the short and long term, is a critical consideration. Although VA was not significantly different between groups by 12 weeks and over 2 years, there was a difference in VA at 4 weeks favoring initial vitrectomy with PRP. Therefore, patients who want to hasten their visual recovery may choose vitrectomy. This early benefit may be most pronounced in eyes with a baseline VA worse than 20/800, presumably due to dense vitreous hemorrhage. Faster visual recovery may be important for patients who are functionally monocular and rely on vision from the eye with vitreous hemorrhage. In this cohort, 26% of participants had VA in the fellow eye that was worse than 20/40 at baseline, emphasizing the need for prompt VA recovery.

Clinicians and patients may initiate treatment with vitrectomy and PRP for patients seeking to minimize future visits and injections. Compared with initial aflibercept, initial vitrectomy and PRP resulted in fewer visits (median, 19 vs 12) and injections (mean, 9 vs 2) over 2 years.[3] Unlike anti-VEGF therapy, vitrectomy directly removes vitreoretinal traction. Release of traction and the performance of endolaser may contribute to the lower likelihood of recurrent vitreous hemorrhage and persistent retinal neovascularization in the vitrectomy group. The presence of neovascularization did not appear to substantially affect VA; however, VA was worse in eyes for which the fundus could not be completely assessed (usually due to vitreous hemorrhage).

Anti-VEGF therapy could be preferable for individuals who prefer in-office procedures to intraocular surgery and its attendant risks, are unable to receive medical clearance for intraocular surgery, have concomitant diabetic macular edema (DME) requiring anti-VEGF treatment, or have limited access to vitreoretinal surgery. Furthermore, PRP damages peripheral visual fields.[2,6] This study provides reassurance that VA outcomes with either approach are, on average, similar from 12 weeks through 2 years.

Based on the Protocol AB results, rates of cataract development and anti-

VEGF treatment for DME may not contribute to the risk-benefit comparison between initial aflibercept vs vitrectomy and PRP. Increased rates of cataract have been reported after vitrectomy,[7] perhaps related to changes in oxygen gradient within the eye.[8] In Protocol AB, however, rates of cataract extraction were not higher with vitrectomy vs aflibercept. Among eyes that underwent cataract surgery, VA was good in both groups. Furthermore, there was no significant difference in the rate of center-involved DME at 2 years, or the proportion receiving aflibercept for DME over 2 years.[3]

One-third of eyes in both groups received the alternative treatment per protocol during 2 years of follow-up. Adherence with long-term follow-up should be stressed because eyes with vitreous hemorrhage from PDR may need supplemental treatment after initial aflibercept or vitrectomy with PRP.

Limitations

This study has several limitations. First, the analyses were post hoc and involved subgroups with limited sample sizes; therefore, the findings should be considered exploratory. Second, although the anti-VEGF treatment algorithm that was used is based on Network Investigator Group consensus and mirrors previous DRCR Retina Network treatment algorithms for DME and PDR, different results might be obtained with different thresholds for treatment or different anti-VEGF agents. Third, although the protocol required the surgical instrumentation to be 23-gauge or smaller, surgeons were allowed to use their standard surgical approaches to improve the generalizability of the results; thus, the vitrectomy procedure varied between surgeons with regard to the use of intraoperative agents, postoperative filtered air or gas, and additional procedures such as epiretinal membrane or internal limiting membrane peeling. Fourth, in the time-to-event analyses, outcomes may have been recorded earlier in the aflibercept group because eyes were examined more frequently (ascertainment bias). Fifth, results beyond 2 years, especially in eyes treated with anti-VEGF without PRP, are unknown.

Conclusions

The results of this comparative effectiveness study suggest that both intravitreous aflibercept and vitrectomy with PRP are viable first-line options for the treatment of vitreous hemorrhage due to PDR. Although a significant difference was not observed between the treatment groups in the primary outcome of mean VA over 24 weeks, eyes that had initial vitrectomy with PRP had faster recovery of vision when baseline VA was worse than 20/800 and faster clearing of initial vitreous hemorrhage. Approximately one-third of the eyes in each group received the alternative treatment (aflibercept or vitrectomy with PRP). These factors may influence treatment decisions for individual patients who are initiating therapy for vitreous hemorrhage from PDR.

Notes

Supplement.

eFigure 1. Initial Aflibercept Group Treatment Algorithm

eFigure 2. Visual Acuity Categories at 4, 24, and 104 Weeks by Treatment Group and Baseline Vision

eFigure 3. Time to Visual Acuity 20/25 or Better by Treatment Group and Baseline Vision

eFigure 4. Time to Visual Acuity 20/25 or Better by Treatment Group and Baseline Visual Acuity

eFigure 5. Time to First Recurrent Vitreous Hemorrhage by Treatment Group

eFigure 6. Time to Cataract Extraction by Treatment Group

eTable 1. Primary and Secondary Outcomes by Treatment Group

eTable 2. Visual Acuity Outcomes by Treatment Group and Baseline

Visual Acuity Subgroups

eTable 3. Visual Acuity and Cataract Extraction by Treatment Group

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References

1. Lightman S, Towler HM. Diabetic retinopathy. *Clin Cornerstone*. 2003;5(2):12-21. doi: 10.1016/S1098-3597(03)90015-9 [PubMed] [CrossRef] [Google Scholar]
2. Gross JG, Glassman AR, Liu D, et al.; Diabetic Retinopathy Clinical Research Network . Five-year outcomes of panretinal photocoagulation vs intravitreous ranibizumab for proliferative diabetic retinopathy: a randomized clinical trial. *JAMA Ophthalmol*. 2018;136(10):1138-1148. doi: 10.1001/jamaophthalmol.2018.3255 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
3. Antoszyk AN, Glassman AR, Beaulieu WT, et al.; DRCR Retina Network . Effect of intravitreous aflibercept vs vitrectomy with panretinal photocoagulation on visual acuity in patients with vitreous hemorrhage from proliferative diabetic retinopathy: a randomized clinical trial. *JAMA*. 2020;324(23):2383-2395. doi: 10.1001/jama.2020.23027 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
4. World Medical Association . World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194. doi: 10.1001/jama.2013.281053 [PubMed] [CrossRef] [Google Scholar]
5. Jaeb Center for Health Research. DRCR.net public web site. Date. Accessed February 25, 2021. http://www.drcr.net
6. Maguire MG, Liu D, Glassman AR, et al.; DRCR Retina Network . Visual field changes over 5 years in patients treated with panretinal photocoagulation or ranibizumab for proliferative diabetic retinopathy. *JAMA Ophthalmol*. 2020;138(3):285-293. doi: 10.1001/jamaophthalmol.2019.5939 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

8. Holekamp NM, Shui YB, Beebe DC. Vitrectomy surgery increases oxygen exposure to the lens: a possible mechanism for nuclear cataract formation. *Am J Ophthalmol*. 2005;139(2):302-310. doi: 10.1016/j.ajo.2004.09.046 [PubMed] [CrossRef] [Google Scholar]